

COMPARISON OF EFFECT OF BROMELAIN AND ACECLOFENAC ON POST-OPERATIVE SEQUELAE FOLLOWING SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLAR – A CLINICAL TRIAL.

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Abstract: Background ∴ Impacted mandibular third molar removal is one of most commonly practiced minor oral surgical procedure performed by oral surgeons. It causes injury to the highly vascularized area, causing complications like pain, swelling and trismus. Bromelain, a botanical enzyme leads to significantly decrease the sequelae after removal of impacted third molar. **Aim:** Comparison of efficacy of bromelain and aceclofenac to reduce post-operative complications after removal of third molar. **Material and methods** : Patients having impacted third molar selected for study. The sample population is 72 and will be divided in 2 groups, each consisting 36 patients. Group 1 will be prescribed with Bromelain capsules 250 mg TDS for 5 days and Group 2 will be prescribed Tab. Aceclofenac BD for 5 days. The sequelae of mandibular third molar surgery include pain, swelling and trismus is measured in two groups and data collected. **Expected Results** : Student's unpaired t-test will be analyse the data from the on 1st ,3rd and 7th day postoperatively . A comparison of both drugs will be achieved by unpaired t-test. The variables include pain, swelling and trismus. When all the parameters will be compared till six postoperatively, the bromelain shows significant results in reducing post-op complications like pain, edema and trismus in removal of impacted third molar. **Conclusion** : Bromelain said to have greater efficacy than Aceclofenac for reducing sequelae like pain, swelling and trismus after impacted third molar surgery.

Keywords- Impacted third molar, Mandibular third molar, Bromelain, Aceclofenac.

INTRODUCTION

Impacted mandibular third molar removal is one of most commonly practiced minor oral surgical procedure performed by oral surgeons. Injury to area of highest vascularity causes complications like pain, edema and trismus. Different modalities have been attempted to reduce the postoperative complications by pharmacologic manipulation to alter the inflammatory response. In order to avoid or minimize post surgical complications surgeons have either modified surgical techniques, such as using lasers and cryotherapy, or advised the patients to use proteolytic enzymes, such as trypsin, chymotrypsin, papain, serratiopeptidase, and bromelain (pineapple enzyme), along with routine antibiotics, analgesics, and corticosteroids.

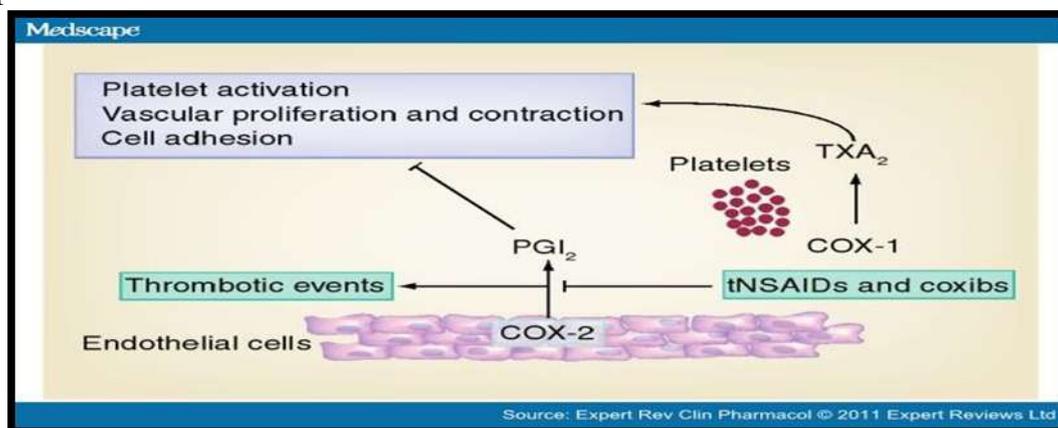
Nonsteroidal anti-inflammatory drugs (NSAIDs) has proven greater results in reducing pain after third molar surgery. Nevertheless, NSAIDs have numerous side effects including haematological disorder, renal impairment and gastrointestinal disturbances and likely cause mucositis and dermatitis.

A botanical proteolytic extract, Bromelain derived from pineapple (*Ananas comosus*) came to existence in late 1957.^{1,2,3} Bromelain has an anti-inflammatory, anticoagulant, antibiotic and antimetastatic property.⁴ The main action of bromelain is anti-inflammatory⁵ Some studies suggests that Bromelain acts by inhibiting the leukocyte migration and adhesion by reducing concentration of cyclo-oxygenase- 2 enzyme.⁶

Bromelain stem have more number of uses as compare to its fruit.^{7,8} Bromelain can have variety of applications in fibrinolysis, aggregation of platelet, anticancer drug, immune modulator also mucolytic in nature.^{9,10,11} Bromelain, botanical extract derivative pineapple plant. The proteolytic action of bromelain have effect as an anti- inflammatory to reduce the complications after removal of third molar . The optimal temperature for enzymatic activity of bromelain is 37°C and pH between 6.5 and 7.5 .¹²

In-vitro studies have been performed by using bromelain orally as an anti-inflammatory and analgesic drug. Bromelain acts by blocking bradykinin and its action on synthesis of prostaglandin resulting in anti-inflammatory action. Bromelain gained interest of drug in field of cosmetic surgery due to its antiedemic, anti-inflammatory, and anticoagulation properties. It aids in healing post-operatively and more potent when used orally. The oral enzymes preparations containing bromelain, rutoside trihydrate ,suggested to have analgesic and anti-inflammatory and anti-oxidants property. Bromelain shows significant results in reducing the pain, edema and trismus after removal of third molar.¹³

We hypothesized that bromelain— in dose of 250 mg started one day before surgery and continued for 4 days—would provide a significant reduction in the postoperative complications after removal of third molar than aceclofenac.



AIM:

To compare and evaluate efficacy of a Bromelain v/s Aceclofenac in management of postoperative pain and swelling after removal of third molar.

OBJECTIVES:

- Evaluation of efficacy of Bromelain and Aceclofenac to reduce pain in post-operative Third molar surgery.
- Evaluation of efficacy of Bromelain and Aceclofenac to reduce swelling in post-operative Third molar surgery
- Evaluation of efficacy of Bromelain and Aceclofenac to reduce trismus in post-operative Third molar surgery

METHODOLOGY:

It will be a hospital based prospective and experimental study..

STUDY DESIGN: Clinical trial.

Student's unpaired t-test will be analyse the data from the on 1st, 3rd and 7th day postoperatively . A comparison of both drugs will be achieved by unpaired t-test. The variables include pain, swelling and trismus. When all the parameters will be compared till six postoperatively, the bromelain shows significant results in reducing post-op complications like pain, edema and reduced mouth opening after removal of third molar.

DURATION: 2 years (from October 2019 to 2021)

SAMPLE SIZE: Total patients – 76

$$SS = \frac{Z^2 * (p) * (1-p)}{c^2}$$

Where,

Z= Z value (e.g: 1.96 for 95% confidence level)

p= percentage picking a choice expressed as a decimal

c= confidence interval, expressed as a decimal

Correction for finite population:

ss

$$\text{new ss} = \frac{ss-1}{1 + \frac{ss-1}{\text{pop}}}$$

where, pop= population

INCLUSION CRITERIA:

- 1) Age group : 15- 60 years.
- 2) Patients having impacted third molar.
- 3) Absence of any systemic pathological conditions.
- 4) Absence of any drug history leading to any periodontal diseases and conditions

EXCLUSION CRITERIA:

- 1) Acute infection in relation to third molar
- 2) Patient having Pine-apple allergy.
- 3) Periapical pathology
- 4) Severe periodontal disease
- 5) Uncontrolled systemic diseases.

6) Debilitating disease.

ARMAMENTERIUM USED IN STUDY:

1. Local Anaesthesia
2. Diagnostic Instruments- Mouth Mirror, Probe
3. Moon's Probe
4. Periosteal Elevator (Molt No. 9)
5. Bard Parker Handle and Scalpel Blade No. 15
6. Backhaus Towel Clip Forceps
7. Jones/Doyens Clip Forceps
8. Artery forceps (straight and curved)
9. Mouth Prop
10. Bone file
11. Needle holder
12. Suture material and needle
13. Tissue cutting scissors and suture cutting scissors
14. Addison's tissue holding forceps
15. Suction tip
16. Micromotor and Handpiece
17. Burs – straight fissure and round

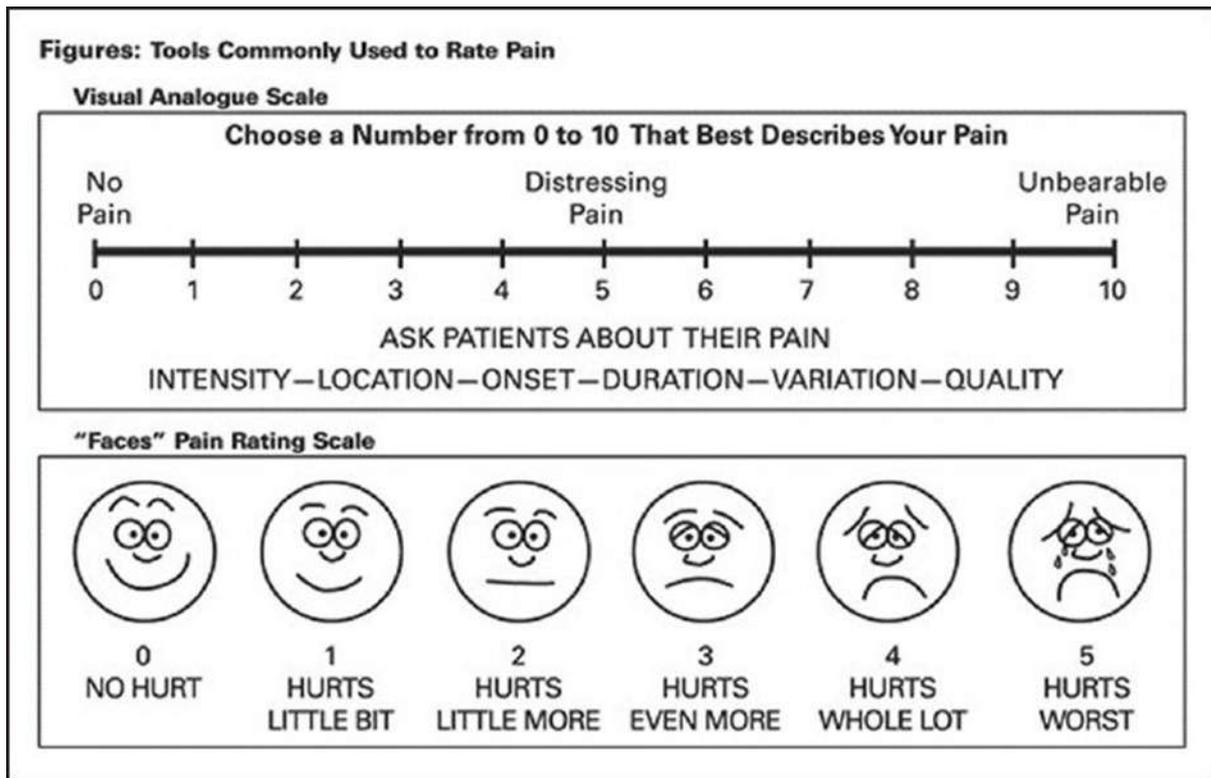
METHODOLOGY:

The study design encompasses prescription of Bromelain tablets to one group and Aceclofenac to other group. Basic blood investigations i.e. HB, BT,CT,RBS will be done, if value are within normal unit then further procedure performed. After the Xylocaine sensitivity test, Lignocaine with Adrenaline administered (2% lignocaine with 1:1,80,000) After negative aspiration, the solution will be administered at a rate of 1ml per minute.

After injecting and achieving all sign and symptoms of local anesthesia, disimpaction will be done by standard surgical protocol. Post operatively, patients will be advised to take Cap Bromelain 2400 GDU/g (Simply Nutra) thrice daily one day prior and continue for three days post-operatively for one group and Tab. Aceclofenac 100 mg twice daily for three days for second group.

Intensity of the achieved anesthesia will be determined by assessment of pain felt during the surgery, recorded by visual analogue scale. The subjective and objective signs and symptoms was assessed by numbness over lip and tip of tongue. For subjective assessment of pain, visual analog scale (VAS) will be used. The point 1 indicates minimal discomfort to level of maximum pain that is unbearable indicated by point 10.

The scores of pain will be recorded on the 1st ,3rdand 7thday postoperatively. Postoperative pain assessment on 1st ,2nd and 3rdday, Facial swelling on first, third and seventh day, and trismus on 1st ,3rdand 7thday. Trismus can be measured by inter-incisal opening. To assess the edema over face measurements taken will be : Menton to Angle, Angle to tragus , and tragus to menton. The observer will be independent and blind to the used drug so as to avoid the bias.



Clinical Variables

- Pre-operative facial measurements will be measured.
- Pain and swelling will be evaluated on days 2 and 7 postoperatively.
- Postoperative pain will be assessed using a Visual Analogue Scale
- Postoperative swelling will be measured by taking mean of distance between tragus and menton base and along ala tragal line using a measuring scale or tape
- Post operative mouth opening measured by scale to check trismus.
- Pre-operative measurements will be compared with post-operative result

PRIMARY OUTCOME :

To evaluate post-surgical pain in third molar surgery.

SECONDARY OUTCOME :

To evaluate post-surgical edema and reduced mouth opening after removal of third molar.

EXPECTED OUTCOME:

Bromelain said to have greater efficacy than Aceclofenac for reducing post-surgical sequelae like pain, edema and reduced mouth opening after removal of third molar.

DISCUSSION:

Majid O W, Adil Al-Mashhadani B.(2014).

Third molar removal is common surgical procedure carried out by oral surgeons. It causes injury to vascularised tissue and cause the inflammatory reaction leading to pain, oedema and reduced mouth opening. Different modalities explained to reduce the complications which include use of NSAIDs. A botanical enzyme, Bromelain derived from pineapple plant, *Ananas comosus*. Proteolytic action of bromelain made it anti-inflammatory in nature¹⁴.

Maria de Souza G , Fernandes I A , Santos C R R, Falc S G M.(2018).

This study evaluated bromelain's efficacy in minimizing post surgical complications including pain , facial edema and reduced mouth opening after removal of third molar. The study concluded that bromelain is effective in controlling post- surgical complications in third molar surgery, more researches are needed¹⁵ .

Ghensi P, Cucchi A, Creminelli L, Tomasi C, Zavan B and Maiorana C (2017).

The study assessed the efficacy of oral bromelain dose to minimize post surgical sequelae of third molar surgery. 84 patients, who required disimpaction of third molar were selected and randomly assigned to 4 groups. First group received no medications, 2nd group was prescribed 40 mg bromelain, 3rd group was prescribed 4 mg dexamethasone sodium phosphate as a submucosally before surgery while last group was prescribed 4 mg dexamethasone sodium phosphate submucosally plus 40 mg bromelain before and after surgery. A follow-up questionnaire assessed patient according to severity of the symptoms. Bromelain proved as a moderately acting anti-inflammatory drug. The combination of bromelain with dexamethasone sodium phosphate show significantly better outcome to control of postsurgical complications¹⁶ .

Singh T, More V, Fatima U, Karpe T, Aleem M A, J. Prameela. (2016).

Randomised control trial was conducted on sample size of 40 subjects required third molar surgery. All patients administered with bromelain along with amoxicillin pre-operatively. Follow up was done on 1st , 3rd , 7th day for assessment of pain VAS sc and assessment of edema using tragus and pogonion as reference points. Posthoc Bonferroni test for pain assessment after surgery on 1st , 3rd , 7th day .They concluded enzymatic activity of bromelain is efficacious to minimize the post surgical outcome for patients undergoing third molar surgery¹⁷ .

Barrera-Núñez M C , Yáñez-Vico R M , Batista-Cruzado A , Heurtebise-Saavedra J M, Oyagüe R C , Lagares D T. (2014).

A cohort study was conducted on 34 subjects. Pre- and postoperative outcomes assessed on 3rd and 8th day. The parameters were inflammation, pain and oral aperture and requirement for pain relievers. 1st group was prescribed Bromelain with a dose of 150mg for 3 days and 100mg from fourth to seventh day, while the other one was prescribed with same dose of placebo in the same dosage. The Mann-Whitney U test was used to assess non-parametric data. They hypothesized that bromelain is more effective than the placebo drug, but for complete evaluation of drug dosage and administration form more studies were needed¹⁸ .

Mende M L T, Nascimento-Júnior E M , Reinheimer D M, Martins-Filho P R S. (2018).

The research included the subjects undergoing third molar surgery. They included 2 groups, one was prescribed bromelain and other was placebo or no-treatment control group. They evaluated the pain, edema and trismus as well as the consumption of analgesics. Current studies suggested that Bromelain is an effective drug in reducing post- surgical complications in third molar surgery¹⁹ .

Liu S, Zhao H, Wang Y, Zhao H and Chuan. (2019).

The study conducted to evaluate effectiveness of bromelain in minimizing post surgical sequelae . Data until November 1, 2017 was collected . Comparison done between two

groups, one of which was prescribed bromelain while other as prescribed placebo drug. The results assessed pain, edema, and reduced mouth opening. Bromelain proved its efficacy in reducing post surgical complications after removal of impacted third molar²⁰.

Isola G&MatareseM&RamagliaL&Iorio-Siciliano V &CordascoG&Matara G.(2018).

This study conducted on 82 subjects undergoing removal of impacted third molar were selected and divided in 3 groups by randomization. First group was given placebo, second group was given ibuprofen and to the third group phytotherapeutic drug was given. They recorded the mouth opening and contour of face between baseline on 1, 3, 7, 10 days after removal. They concluded effect of botanical derivatives were more effective to reduce post surgical complications in removal of third molar²¹.

Few related articles on third molar surgery were reported²²⁻²³⁻²⁴.

CONCLUSION:

Bromelain, botanical enzyme derived from *Ananas comosus* is an active anti-inflammatory action. Its main active ingredient include a number of enzymes having proteolytic action. Bromelain said to have greater efficacy than Aceclofenac for reducing post-operative sequelae like pain, edema and reduced mouth opening after removal of impacted third molar.

LIMITATIONS:

1. A split mouth study design is a desirable model for assessment of potency of any drug given for its assessment.
2. Limited sample size.

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	Group 1	Group 2	Difference*
Mean	2.4	1.6	0.8
Standard deviation	1.5	0.9	
Variance	2.25	0.81	

Sample size of Group 1	38
Sample size of Group 2	38
Total sample size	76

*Difference between the means

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